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Dynamic [2]Catenation of Pd(II) Self-assembled Macrocycles in Water

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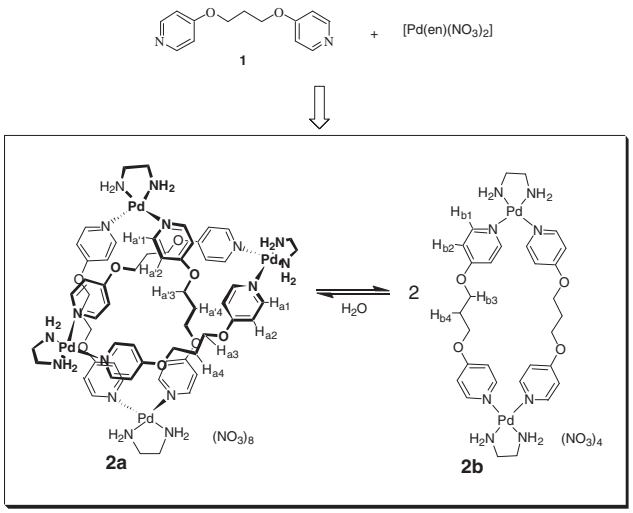
A catenated structure is formed through dynamic self-assembly of 1,3-bis(4-pyridyloxy)propane and cis-protected Pd(II) metal with ethylenediamine in water. ^{1}H NMR spectra have revealed that the formation of [2]catenane is dependent on the concentration of macrocyclic ring. We have performed the structural analysis of macrocyclic ring and [2]catenane using H–H COSY and ESI MS. The dynamic process of the catenation has been elucidated by van't Hoff plot and the formation of [2]catenane is enthalpically favored in D_2O, strongly suggesting the hydrophobic interactions for the formation of [2]catenane. Diffusion-ordered NMR spectroscopy (DOSY) distinguishes between dinuclear self-assembled macrocyclic ring and [2]catenane, indicating that [2]catenanes diffuse slower than macrocyclic rings in D_2O.

Molecular catenanes have drawn a variety of attractions in material-based research fields,[1] since they provide potential for developing molecular functional devices such as molecular sensors[2] and machines[3] in nanosized dimension. Many chemists have explored a number of catenane structures, demonstrating performances with conceptual applicability.[4] Hence, catenated structures have been approached with diverse synthetic strategies and are employed by noncovalent interactions such as hydrogen bonding,[5] donor–acceptor of π electrons,[6] and metal coordination[7] as an interlocking driving force.

Dynamic self-assembly has been utilized as an intriguing approach for the facile formation of catenane structures and, in particular, Pd(II) metal-coordinated self-assembly with appropriate ligands provides opportunity for dynamic formations of catenane, taking advantage of the lability of Pd–N bond in aqueous media.[1b,8]

Since the spontaneous formation of catenated structures using cis-protected Pd(II) metal was reported by Fujita's group,[9] self-assembly of catenanes has been enormously exploited in terms of dynamic mechanism and unique structural features. In aqueous media, most of the Pd(II)-mediated catenanes are thermodynamically assembled under the reversible coordination of Pd–ligand bond and seem to be geometrically interlocked by π–π stacking interaction between macrocyclic ring components. The aromatic group of the catenated macrocyclic ring component is included in the cavity of self-assembled macrocyclic ring. We describe a dynamic formation of catenated structure via Pd(II) metal-coordinated self-assembly. In our system, ligand molecules do not have additional aromatic groups except for the pyridine moiety to be coordinated with Pd(II) metal, and the cavity size of macrocyclic ring is relatively small and is structurally fit to the inclusion of alkyl moiety of counterpart ligand skeleton. Furthermore, it is interesting to note that the cavity of our macrocyclic ring might exhibit the significant affinity for aliphatic guest, which is comparable to the association constant of α-cyclodextrin.



Scheme 1. Dynamic Pd(II) mediated, self-assembly of [2]catenane **2a** and macrocyclic ring **2b**.

Ligand **1** was prepared from 4-chloropyridine hydrochloride and 1,3-propanediol in the presence of excess amounts of NaH according to the previous report[10] and treated with equimolar amounts of [Pd(en)$(NO_3)_2$] in D_2O to afford 1:1 ligand-to-Pd(II) ratio complex (Scheme 1). Generally, Pd(II) metal-mediated self-assembly shows dynamic structural features and the structural reorganizations according to its concentration have been extensively studied in aqueous media.[11] From the former study, we expected that the 1:1 ligand-to-Pd(II) ratio complex may be present as a series of oligomeric species in D_2O. However, the single ^{1}H NMR set of the 1:1 ligand-to-Pd(II) ratio complex implied the formation of single component (Figure 1a) at low concentration (1 mM by **1**) without any oligomeric structures.

The single proton NMR set might correspond to a dinuclear macrocyclic ring rather than high ordered complex structures (e.g., trimeric or tetrameric structures etc.), since the formation of dinuclear macrocyclic ring is entropically more favorable and dominant at low concentration in a similar system.[11b,11c] The structural changes of the 1:1 ligand-to-Pd(II) ratio complex were monitored in the concentration-dependent ^{1}H NMR spectra (Figure 1). As ligand **1** concentration is increased from 1 to 20 mM, a new ^{1}H NMR set appeared gradually and no more complex species seemed to be present in even higher concentration. The new NMR species at higher concentration was characterized by ^{1}H NMR, H–H COSY, and identified as a [2]catenane structure. In ^{1}H NMR and H–H COSY, the proton of a pyridyl ($H_{a'2}$) is observed at considerably higher field, 5.86 ppm, compared to the other peaks. Surprisingly, high upfield shift of alkyl moieties ($H_{a3}/H_{a'3}$ and $H_{a4}/H_{a'4}$) is observed in ^{1}H NMR, implying the alkyl group is located inside

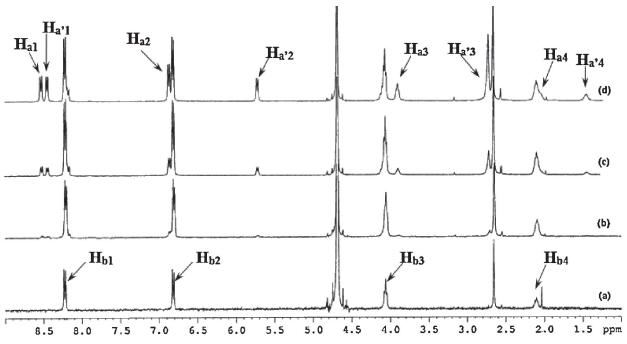


Figure 1. The concentration-dependent ^{1}H NMR spectra (300 MHz, D_2O, 25 °C) monitoring the dynamic equilibrium behaviors between [2]catenane **2a** and macrocyclic ring **2b**. (a) 1, (b) 5, (c) 10, and (d) 20 mM.

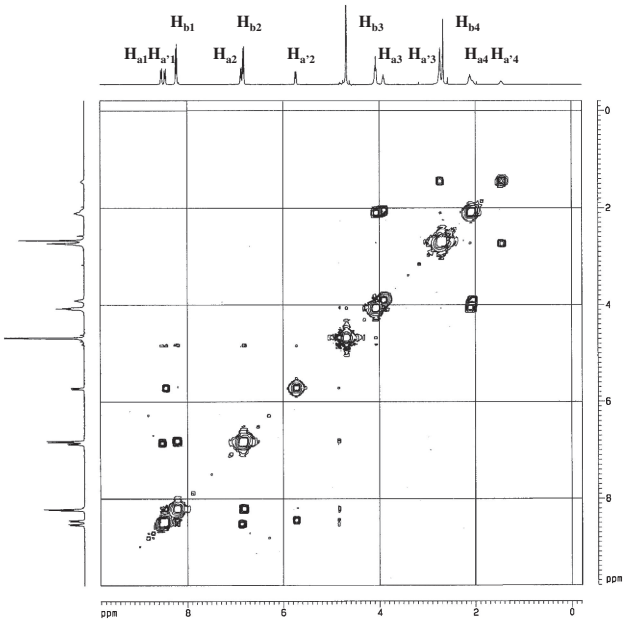


Figure 2. H–H COSY spectrum (300 MHz, D_2O, 20 mM) of [2]catenane **2a** and macrocyclic ring **2b**.

the cavity of a macrocyclic ring component (Figure 1d and Figure 2). In general, high-field shift of pyridine ligand in ^{1}H NMR spectrum is characteristic of catenane structure, i.e., topologically shielded protons of catenanes are observed at a relatively upfield region.[9,12]

Molecular modeling of a [2]catenane structure shows that one of the alkyl groups in a macrocyclic ring is included in the cavity of the other macrocycle (Figure 3a). On the other hand, the double-splitting of H–H COSY ($H_{a1}/H_{a'1}$ and $H_{a2}/H_{a'2}$ of Figure 2) coincidences with two nonequivalent pyridyl groups of each ring in [2]catenane, which were assigned as a (deshielded) and a′ (shielded).

Since the steric demand of [Pd^{II}(en)] moiety and its small cavity size obstruct the circumrotation between two macrocyclic rings, the ring-shuttling of the [2]catanane locks and the C_2 symmetry of the dinuclear macrocycle breaks in NMR time scale. As a result, two ligands of one self-assembled macrocycle become diastereotopically discriminated in ^{1}H NMR spectra and

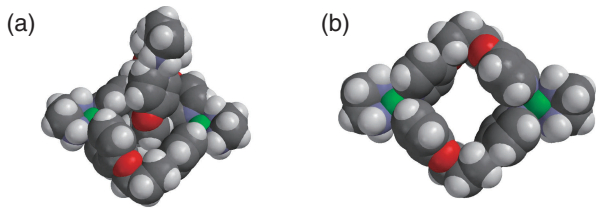


Figure 3. Molecular modeling structures of (a) [2]catenane **2a** and (b) macrocyclic ring **2b**.[13]

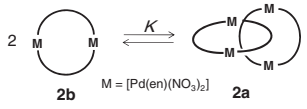
give the unique, double-split pattern. Molecular modeling has revealed that the dinuclear macrocyclic ring has small cavity size (ca. 7 Å) in diameter (Figure 3b).

Dynamic catenation of macrocyclic ring was further verified by ESI MS, diffusion-ordered NMR spectroscopy (DOSY), and van't Hoff analysis. The electrospray ionization mass spectrum (See Supporting Information Figure S1[16]) confirms [2]catenane **2a** and macrocyclic ring **2b**. The quasimolecular ions of [2]catenane **2a**, m/z 632, 458, 337, 285, 235 which correspond to $[M - 3(NO_3)]^{3+}$, $[M - 4(NO_3)]^{4+}$, $[M - 5(NO_3) - (HNO_3)]^{5+}$, $[M - 6(NO_3)]^{6+}$, $[M - 7(NO_3)]^{7+}$ respectively, were observed in ESI MS. Whereas the quasimolecular ions (m/z) with even number are also attributed to macrocyclic ring **2b** as well as [2]catenane **2a**, the observed fragment ions with odd numbers confirm the formation of [2]catenane. DOSY study (See Supporting Information Figure S2[16]) has revealed that both [2]catenane **2a** and macrocyclic ring **2b** diffuse more slowly compared to small molecule, HOD as an internal reference and self diffusion rates of two species are slightly different in D_2O, indicating that [2]catenane (2.51×10^{-10} m^2 s^{-1}) moves slower than the macrocyclic ring (3.16×10^{-10} m^2 s^{-1}). From the Stokes–Einstein equation,[14] the hydrodynamic radius of macrocyclic ring and [2]catenane are determined to be 6.30 and 7.39 Å, respectively, which are significantly comparable to the calculated molecular radius in molecular modeling (Figure 3).

To define thermodynamic parameters controlling the catenation process, the van't Hoff analysis (Figure 4) of the association constants between [2]catenane **2a** and macrocyclic ring **2b** was carried out variable temperature ^{1}H NMR experiments (See Supporting Information Figure S3[16]), which additionally confirmed the dynamic equilibrium between [2]catenane **2a** and macrocyclic ring **2b**. The catenation process is enthalpically favored ($\Delta H° = -10.5$ kcal mol^{-1}) and entropically less favored ($\Delta S° = -15.7$ cal K^{-1} mol^{-1}). The enthalpically driven catenation indicates that the hydrophobic interactions between macrocyclic rings contribute to the formation of catenated structure **2a**. In other words, the hydrophobic cavity of macrocyclic ring **2b** results in the inclusion of the counterpart macrocycle skeleton. Eventually, the hydrophobic interaction between the ligands allows the two macrocyclic rings **2b**s to form a [2]catenane **2a** in water.

In order to support the formation of dinuclear macrocyclic ring and testify the macrocyclic cavity, *n*-butanol is employed as a small organic guest and ^{1}H NMR titrations (See Supporting Information Figure S5[16]) are carried out. In a low concentration (2 mM), where macrocyclic ring is solely present, macrocyclic ring has significant binding affinity ($K_a = 50$ M^{-1}) for *n*-butanol in D_2O, which is comparable to the affinity of α-cyclodextrin (α-CD),[15] implying **2b** is similar to α-cyclodextrin in the cavity size.

(a)



$\Delta H°$/kcal mol^{-1}	$\Delta S°$/cal K^{-1} mol^{-1}	$\Delta G°^{(300K)}$/kcal mol^{-1}
−10.5	−15.7	−5.7

(b)

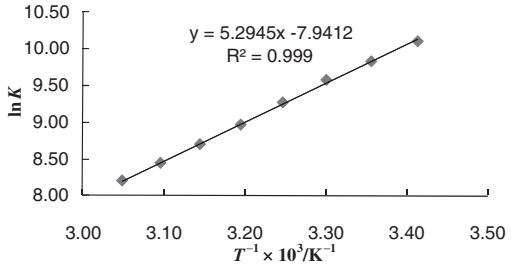


Figure 4. Thermodynamic parameters (a) and van't Hoff analysis (b) of dynamic catenation process of macrocyclic ring **2b**.

In conclusion, the Pd(II) metal-mediated self-assembly of sterically restricted bispyridyl ligand **1** results in the dynamic [2]catenation of macrocyclic ring, which is enthalpically driven by the hydrophobic attraction. Its dynamic equilibrium between macrocyclic ring and [2]catenane is observed in the concentration- and temperature-dependent ^{1}H NMR experiments. Diffusion-ordered NMR spectroscopy (DOSY) shows that the dynamically self-assembled, [2]catenane and macrocyclic ring gives two different DOSY sets according to each diffusion rate in D_2O. The observed diffusion rates of two dynamic supramolecular structures could be interpreted in the perspective of molecular volumes. The self-assembled macrocyclic ring has an appropriate cavity which allows for self-catenation and, additionally, provides room for including guests with aliphatic group, like *n*-butanol.

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16 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

